

**Amendments to the Drawings:**

The Examiner objects to the disclosure because the data presented in Figure 3 does not correspond to its description in the Brief Description of the Drawings and the specification at page 15. Applicants are filing herewith a replacement set of drawings, which now includes Figures 1A-B, 2 and 3.

**Remarks/Arguments**

**Status of the Claims**

The Examiner notes that the preliminary amendment filed on September 22, 2005 incorrectly recites the priority claim of the present application. Applicants have amended the specification to recite that the present application is a national stage application of International Application No. PCT/ US2003/27618, which designated the United States and was filed on September 4, 2003, which claims the benefit of United States Patent Application Serial Number 10/392,333, filed March 19, 2003. The provisional applications are retained in the paragraph to ensure that the incorporation by reference is maintained.

Claims 1, 2, 4-8, 10-16, and 18-28 are pending in the application. Reconsideration is respectfully requested.

**Specification**

The Examiner objects to the disclosure because the data presented in Figure 3 does not correspond to its description in the Brief Description of the Drawings and the specification at page 15. Applicants are filing herewith a replacement set of drawings. These are the drawings that were originally filed in the PCT office on September 4, 2003. In response to the Invitation to Correct the Drawings, Applicants filed substitute sheets of these drawings and one sheet was inadvertently not included in the published PCT application. This error was on the part of the PCT office and not the Applicants' error, however, that error was not appreciated until the Examiner made note of the discrepancy in the Office Action. The descriptions of the drawings throughout the application now match the enclosed replacement drawings. Withdrawal of the objection is respectfully requested.

**Claim Rejections-35 U.S.C. §112**

The Examiner has rejected claims 5, and 11-20 under 35 U.S.C. §112, second paragraph as being indefinite. The Examiner states that claim 5 recites the limitation *trospium hydrochloride* and that there is insufficient antecedent basis for the term

“hydrochloride” in claim 1 from which claim 5 depends. The rejection is not understood. Claim 5 is a proper dependent claim that further defines the subject matter of claim 1. Of course, a dependent claim can introduce words that are not found in an earlier claim. The presence of such a word does not raise antecedent basis problems. Claim 1 recites a method for treating a disease comprising administering via inhalation a pharmaceutical composition comprising trospium. Claim 5 further defines the pharmaceutical composition comprising trospium as being an aqueous composition comprising trospium in the form of trospium chloride. As such, the formulation of claim 5 comprises trospium, as well as hydrochloride. One reading the specification would reasonably conclude that the term “trospium” also embraces salts thereof. Therefore, claim 5 is written in proper dependent claim format and the rejection is improper. Withdrawal of the rejection is respectfully requested.

The Examiner states that the term “fine particle fraction” in claim 8 is indefinite because any particle size will satisfy the limitation of this claim. The term “fine particle fraction” is clearly defined on page 4, line 1 of the present specification as “the mass of the composition that possesses an aerodynamic diameter of less than 3.4 microns as determined with an 8 Stage Anderson Cascade Impactor, used according to manufacturer’s specifications”. Therefore, the meaning of this term is clear in the context of the claim in view of the specification and the rejection is improper. Withdrawal of the rejection is respectfully requested.

The Examiner states that the term “less than” in claims 11, 12, and 15 renders the claims indefinite because it does not set a lower limit. As an example the Examiner points to claim 15 which is drawn to the formulation of claim 14 wherein said formulation contains less than 10% by weight of trospium. The Examiner concludes that since no lower limit is set the formulation can have 0% trospium. Given that claim 15 ultimately includes all of the limitations of claim 1, and claim 1 requires that the composition comprise trospium, the skilled practitioner would immediately realize that 0% trospium would fall outside the scope of the broadest claim 1 from which claim 8 ultimately depends. Further, the amount needs to be sufficient to achieve the stated therapeutic effect, upon considering the total amount of product delivered. Furthermore, in accordance with MPEP 2173.05(b):

the fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.

One skilled in the art would clearly understand from the specification what is meant by phrase “less than 10% by weight of trospium” based on the present application. On page 4, lines 27-31, of the present application, it is taught that the concentrations of about 1%, about 4% or about 5% are specifically contemplated. Thus, the specification provides the skilled person with adequate information with which to assess the scope of the relative term and thereby be reasonably apprised of the scope of the invention. Indeed, the use of the term “less than” is commonplace in US patent claims. The term is found in the claims of more than 400,000 granted patents granted since 1976. The scope of the claim is clear and the rejection improper. Withdrawal of the rejection is respectfully requested.

The Examiner states that the term “at least” in claim 14 renders the claim indefinite as no upper limit is defined. Applicants respectfully disagree. One skilled in the art would be reasonably apprised of the scope of the claim in light of the present specification. For example, Table 1 on page 10 provides trospium formulations comprising 85% and 90% leucine. Clearly the upper limit has to be something less than 100% as the composition is required by the claims to also have trospium. Therefore, the specification provides the skilled person with adequate information with which to assess the scope of the relative term and thereby be reasonably apprised of the scope of the invention. The scope of the claim is clear and the rejection improper. Withdrawal of the rejection is respectfully requested.

### Claim Rejections-§102

The Examiner has rejected claims 1, 2, 6-8, 10-13, 15, 22-24 and 26-28 under 35 U.S.C. §102(a) as being anticipated by Basu (WO 2003/079885). The rejection is improper. The International Filing Date of the present application is September 4, 2003, which in turn claims priority to USSN 10/392,333, filed March 19, 2003. Both of these

dates are prior to the publication date of Basu on October 2, 2003. Therefore, Basu is not available as §102(a) prior art.

It should be noted that Basu is the published PCT application that corresponds to USSN 10/392,333, the priority document for the present application. The PCT application was filed on the same date as the priority application. Under 35 USC 102(e), the reference can be prior art only for those claims that do not find a valid priority claim in the '333 application. However, the Examiner has not held that any claim is denied priority and such a holding would appear to be inconsistent with a finding that the claims are anticipated.

Therefore, to the extent that the Examiner is correct that the present claims are taught in Basu, the present invention is entitled to the priority of USSN 10/392,333 and Basu is not prior art.

To the extent that one or more of the present claims may be held to not be entitled to priority, the relevant disclosure(s) presented in the PCT application and corresponding '333 application which are specifically described to give rise to an anticipation rejection are not the inventions by another but are the inventions of the present inventors. As such, Basu is not prior art against the present application under 35 USC 102(e).

Withdrawal of all rejections under §102 is respectfully requested.

Claim Rejections 35 U.S.C. §103

The Examiner has rejected claims 1, 2, 4 and 5 under 35 U.S.C. §103(a) as being unpatentable over Freund (U.S. Pat. Pub. No. 2001/0008632) in view of Richards (U.S. Pat. Pub. No. 2003/0158176). The Examiner states that Freund teaches aqueous aerosols of *inter alia* trospium chloride for inhalation in the treatment of respiratory diseases. The Examiner also states that the reference generically teaches doses of between 12 mcg and 2400 mcg for all active agents described. The undersigned believes that the dose range generically taught for all drugs is 1.2 mcg to 2400 mcg.

The Examiner acknowledges that Freund does not teach specific respiratory passage diseases or a specific dose for trospium. It is believed that the Examiner will also acknowledge that the reference does not teach the dose required to achieve a 10 hour therapy by inhalation.

The Examiner then asserts that Richards teaches anticholinergic agents including trospium for treating COPD. The Examiner asserts that Richards teaching that dose depends on many factors and that one of ordinary skill in the art would have optimized the dose taught by Freund to maximize the therapeutic effects of the active agent. The Examiner concludes that it would be obvious to combine Freund and Richards to treat diseases such as COPD by inhalation administration of trospium. Applicants respectfully disagree.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. *See M.P.E.P. §§2143*. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Appellant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed inventions, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Sang Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations and quotes omitted). Additionally, it is now well-established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Kotzab*, 217 F.3d at 1370.

Without the benefit of the present application, the Examiner has provided no motivation as to why one would pick trospium or trospium chloride from the list of over 100 active ingredients disclosed in paragraphs 0015-0045 of Freund in order to prepare an optimized formulation having a sustained effective therapy for at least 10 hours. Even if one were motivated to pick trospium from the exceedingly long list of Freund's possible active agents, Richards would not then motivate the skilled person to seek a trospium formulation having sustained effective therapy for at least 10 hours. The

Examiner's conclusion that mere optimization as taught by Richards would result in the presently claimed invention is entirely unsupported. As stated in MPEP §2143.01:

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art" at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levingood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000).

The Examiner has provided no evidence as to why the skilled person would choose trospium from the long list provided in Freund and then be led by the vague, boiler plate statements in Richards that the "dosage of the specific compound according to the invention will vary depending on its potency, the mode of administration, the age and weight of the patient and the severity of the condition to be treated". Clearly this passage from Richards does not provide the skilled person with any motivation or expectation of success in preparing a formulation of any kind having sustained effective therapy for at least 10 hours, much less a trospium formulation. It should be pointed out that Richard's "compound according to the invention" is not trospium at all, but is instead a novel quaternary ammonium compound disclosed in Richards. Richard's mention of trospium at paragraph 91 is merely in passing to refer the reader to other antimuscarinic compounds already known in the art. Therefore, any discussion in Richards with regard to optimizing therapeutic formulations are with regard to Richard's own compounds and not trospium.

In view of the above discussion, the Examiner has failed to establish a *prima facie* case of obviousness over Freund in view of Richards. Withdrawal of the rejection is respectfully requested.

The Examiner has rejected claims 1, 2, 4, 6-8, 10-16, and 18-28 under 35 U.S.C. §103(a) as being unpatentable over Basu (WO 2003/079885) in view of Richards (U.S. Pat. Pub. No. 2003/0158176). As discussed above, Basu is not available as §102(a) prior art and is instead arguably available only as §102(e) prior art. As such, in view of the

Statement Sufficient to Establish Common Ownership, below, Basu is not eligible as prior art for the purposes of obviousness as per 35 U.S.C. §103(c).

**STATEMENT OF COMMON OWNERSHIP**

**WO 2003/079885 (BASU) AND THE PRESENTLY CLAIMED APPLICATION WERE COMMONLY OWNED AT THE TIME THE CLAIMED INVENTION WAS MADE OR SUBJECT TO AN OBLIGATION OF ASSIGNMENT THAT WOULD ESTABLISH COMMON OWNERSHIP.**

In view of the above Statement of Common Ownership, the Examiner's combination of Basu and Richards is moot. Withdrawal of the rejection under this section is respectfully requested.

**Conclusion**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

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Attachments:  
REPLACEMENT DRAWINGS